Q1 Concluded

c) detecting said detection probe.]

Q2

18. (Amended) A method of detecting at least one target, comprising

a) contacting a sample which may comprise said target(s) with a nuclease protection fragment(s) specific for and which binds to said target(s), exposing the sample to a nuclease effective to digest remaining single strand nucleic acid, and then contacting the resultant sample with a bifunctional linker which has a first portion that is specific for an oligonucleotide anchor and a second portion that comprises a probe which is specific for said [target(s)] nuclease protection fragment(s), under conditions effective to obtain a first hybridization product between said [target(s)] nuclease protection fragment(s) and said linker, and

b) contacting said first hybridization product with a combination under conditions effective to obtain a second hybridization product between said first hybridization product and said combination, wherein said combination comprises, before the addition of said first hybridization product,

1) a surface comprising multiple spatially discrete regions, at least two of which are substantially identical, each region comprising

2) at least [8] two different oligonucleotide anchors[,].

[c) contacting said first hybridization product or said second hybridization product with a labeled detector probe, and

d) detecting said detection probe.]

Please add the following claims:.

Q3

--19. A method of detecting at least one nucleic acid target, comprising contacting a sample which may comprise said target(s) with a nuclease protection fragment(s) specific for and which binds to said target(s), thereby forming a nuclease protection fragment/target duplex, exposing the sample to a nuclease effective to digest remaining single strand nucleic acid, and then contacting the resultant sample with a combination which comprises, before the addition of said sample,

i) a surface comprising multiple spatially discrete regions, at least two of which are substantially identical, each region comprising

ii) at least two different anchors, each in association with

iii) a bifunctional linker which has a first portion that is specific for the anchor, and a second portion that comprises a probe which is specific for a portion(s) of said duplex,

Q3

under conditions effective for hybridization,

and detecting any bound protected portion(s).

20. The method of claim 15, wherein each region comprises at least about four different oligonucleotide anchors.

21. The method of claim 15, wherein each region comprises at least about eight different oligonucleotide anchors.

22. The method of claim 15, wherein each region comprises at least about 64 different oligonucleotide anchors.

23. The method of claim 15, wherein each surface comprises at least about 96 to about 1536 substantially identical, spatially discrete regions.

24. The method of claim 15, wherein each surface comprises about 4-1536 substantially identical, spatially discrete regions, each region comprising about 8 to about 100 different oligonucleotide anchors.

25. The method of claim 15, wherein each surface comprises about 4, 8, 96 or 384 substantially identical, spatially discrete regions, each region comprising about 4 to about 100 different oligonucleotide anchors.

26. The method of claim 15, wherein each of said regions comprises about 30 to about 100 probes, each specific for a different target.

27. The method of claim 15, wherein said regions are further subdivided into smaller subregions.

28. The method of claim 15, wherein each region is a well of a microtiter plate.

29. The method of claim 15, wherein said anchors are oligonucleotides of about 30 to about 50 nucleotides in length.

30. The method of claim 15, wherein one or more regions further comprise controls for hybridization efficiency or specificity.

31. The method of claim 15, wherein one or more regions further comprise controls for the capacity of a locus to bind target.

32. The method of claim 15, further comprising contacting said combination and any bound nuclease protection fragments with a labeled detection probe, and detecting said detection probe.

33. The method of claim 15, further comprising

a) subjecting the sample comprising target(s) bound to nuclease protection fragment(s) to treatment with one or more nucleases effective for digesting nucleic acid other than the nuclease protection fragment(s) which have hybridized to the nucleic acid(s) of interest and, optionally, the portion(s) of said nucleic acid(s) which have been hybridized, and

Q3

b) removing nucleic acid material other than said nuclease protection fragment(s) which have hybridized to said nucleic acid(s) of interest, to provide a sample containing the nuclease protection fragment(s).

34. The method of claim 15, which identifies an RNA expression pattern, wherein at least two of said nuclease protection fragments are specific for different RNA molecules.

35. The method of claim 34, which identifies an agent which modulates an RNA expression pattern, further comprising comparing the RNA expression pattern produced in the presence of said agent to the RNA expression pattern produced under a different set of conditions.

36. The method of claim 15, for identifying an agent which modulates the interaction of said nuclease protection fragment(s) with said probe(s).

36. The method of claim 15, wherein said nuclease protection fragment is DNA.

37. The method of claim 36, wherein the DNA is amplified before said sample comprising said nuclease protection fragment(s) is contacted with said combination.

38. The method of claim 38, wherein said amplification is PCR amplification.

39. The method of claim 15, wherein said nucleic acid target comprises a polymorphism.

40. The method of claim 15, wherein said combination comprises a large number of said regions, and wherein the method is a high throughput method.

41. The method of claim 15, wherein a large number of samples are assayed rapidly.

42. The method of claim 15, further comprising removing said bifunctional linkers from said oligonucleotide anchors and replacing them with substantially identical or with different bifunctional linkers, thereby reprogramming said surfaces, and repeating said method of detecting a target.

43. The method of claim 15, wherein said anchors have been dissociated from bifunctional linkers having a different target specificity.

44. The method of claim 15, wherein said sample is generated *in vitro* or *in vivo*.

45. The method of claim 15, wherein said sample is generated by incubating or growing cells which may contain said target(s) and extracting nucleic acid from the cells.

46. The method of claim 15 which is diagnostic for a disease, which measures a side effect of a drug, or which identifies an agent which has a therapeutic effect.

47. The method of claim 15, which is predictive of a disease, or which measures the efficacy, safety, or metabolism of a drug.

48. The method of claim 15, wherein at least of one said targets is a DNA molecule and at least one of said targets is an RNA molecule.

a3

49. The method of claim 15, wherein at least of one said nuclease protection fragments is specific for a DNA molecule and at least one of said nuclease protection fragments is specific for an RNA molecule.

50. The method of claim 15, wherein said targets are DNA molecules.

51. The method of claim 15, wherein said anchors are oligonucleotide anchors.

52. A method of detecting at least one nucleic acid target, comprising contacting a sample which may comprise said target(s) with a nuclease protection fragment(s) specific for and which binds to said target(s), exposing the sample to a nuclease effective to digest remaining single strand nucleic acid, and then contacting the resultant sample with a combination which comprises,

i) a surface comprising multiple spatially discrete regions, at least two of which are substantially identical, each region comprising

ii) at least two different anchors, each in association with

iii) a bifunctional linker which has a first portion that is specific for the anchor, and a second portion that comprises a probe which is specific for said nuclease protection fragment(s),

under conditions effective for said nuclease protection fragment(s) to bind to said combination,

and detecting said bound protection fragment(s).

53. A kit useful for the detection of at least one nucleic acid target in a sample, comprising

a) at least one nuclease protection fragment specific for said nucleic acid(s), but not for any of the oligonucleotide anchors in said kit,

b) a surface, comprising multiple spatially discrete regions, at least two of which are substantially identical, each region comprising at least two different oligonucleotide anchors, and

c) a container comprising at least one bifunctional linker molecule, which has a first portion specific for at least one of said oligonucleotide anchors and a second portion that comprises a probe which is specific for, and in said detection binds to, at least one of said nuclease protection fragments.

54. The kit of claim 53, further comprising

d) one or more nucleases effective for digesting single strand nucleic acid and/or the RNA strand of a DNA/RNA duplex.

55. A kit useful for the detection of at least one nucleic acid target in a sample, comprising

a) a surface, comprising multiple spatially discrete regions, at least two of which are substantially identical, each region comprising at least two different oligonucleotide anchors,